COVID-19 Therapeutics Information Brief

January 5, 2021

Changes to the document from the previous version are highlighted in yellow.

IMPORTANT/NEW COVID-19 Therapeutics Information

Using Therapeutics to Prevent and Treat COVID-19

The SARS-CoV-2 Omicron variant has quickly become the dominant variant of concern in the United States and is present in all 50 states. The Centers for Disease Control and Prevention (CDC) recommends eligible individuals should receive all vaccines and booster shots as the best preventive measure available against severe disease, hospitalizations, and death due to COVID-19. Therapeutics are also available for preventing and treating COVID-19 in specific at-risk populations. These therapeutics differ in efficacy, route of administration, risk profile, and whether they are authorized by the U.S Food and Drug Administration (FDA) for adults only or adults and certain pediatric populations. Some therapeutics are in short supply, but availability is expected to increase in the coming months. The below information serves to familiarize healthcare providers with available therapeutics, understand how and when to prescribe and prioritize them, and recognize contraindications.

On November 24, 2021, a new variant of SARS-CoV-2, B.1.1.529 (Omicron), was reported to the World Health Organization (WHO). On December 1, 2021, the first case of COVID-19 attributed to

Omicron was reported in the United States. Current CDC recommendations for vaccines and booster shots are expected to protect against severe illness, hospitalizations, and deaths from infection with the Omicron variant. Some studies have found lower effectiveness of the primary series of vaccines against infection and demonstrated the importance of booster doses.

Monoclonal Antibodies

The Omicron variant, with its numerous mutations in the spike protein, is not neutralized by bamlanivimab and etesevimab or casirivimab and imdevimab, the most frequently prescribed monoclonal antibody-based COVID-19 treatments. Despite some reduction in neutralization concentrations, sotrovimab remains effective against all variants of concern, including Omicron. However, sotrovimab is currently in limited supply, and its use should be prioritized for nonhospitalized patients with risk factors for progression to severe COVID-19, including individuals who are unvaccinated, have not received all vaccines and booster shots as recommended by CDC, individuals with clinical risk factors, older age (for example ≥65 years of age), and individuals not expected to mount an adequate immune response. Sotrovimab can be used in these high-risk individuals when Paxlovid (described below) is not indicated due to potential severe drug-drug interactions or if Paxlovid is not available.

Antivirals

- Remdesivir is a nucleoside analog approved by FDA for the treatment of hospitalized patients with COVID-19. A recent randomized placebo-controlled outpatient study evaluated three daily intravenous (IV) infusion of remdesivir given within seven days of symptom onset. This study found that the reduction in hospitalization rates was similar to that achieved by using anti-SARS-CoV-2 monoclonal antibody-based therapy. Remdesivir is expected to be effective against the Omicron variant based on in vitro data; however, in vivo data are currently limited. Outpatient use of remdesivir requires support of IV infusion centers with appropriate skilled staffing.
- Two oral antivirals, Paxlovid (ritonavir-boosted nirmatrelvir) and molnupiravir, are now available under Emergency Use Authorization by FDA for treating COVID-19 in outpatients with mild to moderate disease. Each drug is administered twice daily for five days. There are considerable differences in efficacy, risk profiles, and use restrictions between the two oral antivirals. From their individual clinical trials, compared to placebo, severe outcomes (hospitalization or death) were reduced by 88% for Paxlovid compared to 30% for molnupiravir. Healthcare providers need to be familiar with these distinctions to make clinical decisions and inform patients. In addition, initiating treatment with these oral antivirals must begin within five days of symptom onset to maintain product efficacy. Paxlovid is currently in very limited supply and use should be prioritized for higher risk populations. Due to the potential for severe drug-drug interactions with ritonavir, a medication used for HIV treatment, CDC strongly suggests that healthcare providers not experienced in prescribing Paxlovid refer to the NIH Statement on Paxlovid Drug-Drug Interactions | COVID-19 Treatment Guidelines. Healthcare providers could also contact a local clinical pharmacist or an infectious disease specialist for advice. Like Paxlovid, molnupiravir is expected to be active against all circulating variants of concern, including Omicron. Molnupiravir should only be used when other options are not available, due to its lower efficacy. Molnupiravir use is

not recommended in pregnancy because of potential mutagenicity. Molnupiravir is also not recommended in patients who are breastfeeding or pediatric patients due to limited data within these populations and concerns for potential bone growth toxicity in the young.

Pre-exposure therapeutics for high-risk groups

AstraZeneca's EVUSHELD, which includes two long-acting anti-SARS-CoV-2 monoclonal antibodies, is the only Emergency Use Authorization pre-exposure prophylaxis product available. EVUSHELD is expected to be effective against the Omicron variant; however, treatment effectiveness should be monitored. EVUSHELD is intended for the highest risk immunocompromised patients who are not expected to have an effective response to vaccination. EVUSHELD is indicated for pre-exposure prophylaxis only and not for treatment of patients with COVID-19.

Therapeutic Resources

Bamlanivimab and Etesevimab

- Bamlanivimab and Etesevimab EUA Letter of Authorization (EUA)
- Bamlanivimab and Etesevimab Provider Fact Sheet
- Frequently Asked Questions on the EUA for Bamlanivimab and Etesevimab
- Bamlanivimab and Etesevimab Fact Sheet for Patients and Caregivers

REGEN-COV® (casirivimab and imdevimab)

- REGEN-COV® EUA Letter of Authorization (EUA)
- REGEN-COV® Provider Fact Sheet
- Frequently Asked Questions on the EUA for REGEN-COV®
- REGEN-COV® Fact Sheet for Patients and Caregivers

Sotrovimab

- Sotrovimab EUA Letter of Authorization (EUA)
- Sotrovimab Provider Fact Sheet
- Frequently Asked Questions on the EUA for SOTROVIMAB
- Sotrovimab Fact Sheet for Patients and Caregivers

Evusheld

- Evusheld EUA Letter of Authorization (EUA)
- Evusheld Provider Fact Sheet
- Frequently Asked Questions on the Emergency Use Authorization for Evusheld
- Evusheld Fact Sheet for Patients and Caregivers

Paxlovid

- Paxlovid EUA Letter of Authorization
- Paxlovid Provider Fact Sheet
- Frequently Asked Questions on the Emergency Use Authorization for Paxlovid
- Paxlovid Fact Sheet for Patients and Caregivers

Molnupiravir

- Molnupiravir EUA Letter of Authorization
- Molnupiravir Provider Fact Sheet
- Frequently Asked Questions on the Emergency Use Authorization for Molnupiravir
- Molnupiravir Fact Sheet for Patients and Caregivers

Redistribution Requests for Therapeutics

Requests have been received regarding redistribution of monoclonal antibodies, evusheld and antivirals. A process is being developed at the department and will be shared once tested and approved. In the meantime, healthcare providers with products to redistribute should email the IDPH Therapeutics Call Center at C19Therapeutics@idph.iowa.gov for directions. **Do not redistribute any doses or courses of therapeutics without contacting the Therapeutics Call Center prior to transferring.**

Informational Letter from Iowa Department of Human Services (DHS), Iowa Medicaid Enterprise (IME) Regarding Monoclonal Antibody Reimbursement

The link below is to an informational letter updating providers regarding the appropriate billing and coding fees for the use of Monoclonal Antibodies to treat COVID-19.

- COVID-19 Vaccines and Monoclonal Antibodies Informational Letter, January 2021

Weekly Allocations Cadence for Monoclonal Antibodies, Pre-Exposure Prophylaxis Treatment and Antivirals

The allocation cadence for monoclonal antibodies (REGEN-COV, bamlanivimab/etesevimab, sotrovimab) and the pre-exposure prophylaxis treatment (Evusheld) will shift to a weekly allocation cycle**.** The ordering cadence will be as follows:

- Allocation Survey Sent - Monday
- Allocation Survey Due Back to IDPH - Tuesday at 4:00pm
- Allocation Ordered in Federal System - Thursday
- Allocation Amount Notification from IDPH to healthcare providers - Thursday

The allocation cadence for antivirals will shift to a every other week allocation cycle. The next allocation for antivirals products will be the week of January 10, 2022. The ordering cadence will be as follows:

- Allocation Survey Sent - Monday
- Allocation Survey Due Back to IDPH - Tuesday at 4:00pm
- Allocation Ordered in Federal System - Thursday
- Allocation Amount Notification from IDPH to healthcare providers - Thursday

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Allocations to Partners for Monoclonal Antibodies, Pre-Exposure Prophylaxis Treatment and Oral Antivirals

Local Public Health Agencies and Hospital Partners can refer to the Iowa Health Alert Network (HAN) Therapeutics folder-partner list for the spreadsheet listing the facilities that have been allocated therapeutics for each type of product. IDPH is developing an allocation map that will be available soon.

Bamlanvimab/Etesevimab and REGEN-COV Unlikely to Retain Activity Against Omicron Variant

As Omicron is increasingly circulating in Iowa communities, IDPH encourages healthcare providers to utilize current supplies of bamlanivimab and etesevimab and REGEN-COV as soon as possible while other variants are still causing illness incommunities. While it appears sotrovimab is more effective against Omicron, doses are limited at this time.

Data show it is unlikely bamlanivimab/etesevimab or REGEN-COV will retain activity against this variant. Based on similar cell culture data currently available, sotrovimab appears to retain activity against the Omicron variant.

Beginning the week of January 3, 2022, the Federal COVID-19 Response Team does not plan to allocate bamlanivimab/etesevimab or REGEN-COV to states with greater than 80% prevalence of the Omicron variant (based on CDC NOWCAST data). When allocations of bamlanivimab/etesevimab and REGEN-COV are paused in Iowa, the Iowa Department of Public Health will notify administration sites.

Therapeutic Reporting Reminder

Sites receiving monoclonal antibodies, pre-exposure prophylaxis treatment, or oral antivirals **MUST** comply with reporting requirements in order to receive future allocations. Reporting requirements are as follows:

- Monoclonal antibodies (REGEN-COV, bamlanivimab/etesevimab, sotrovimab): Report on-hand and usage data **every Wednesday** in EMResource (for hospitals), NHSN (for long-term care facilities), or Teletracking (for all other sites).
- Pre-exposure prophylaxis treatment or oral antivirals (Evusheld, Paxlovid, Molnupiravir): Report on-hand and usage data **daily** in HPoP. If you need assistance with HPoP, please contact c19therapeutics@idph.iowa.gov.

Bamlanivimab/Etesevimab Shelf Life Extension Reminder

FDA and ASPR announced the authorization of an extension to the shelf-life from 12 months to 18 months for specific lots of the refrigerated Eli Lilly monoclonal antibodies, bamlanivimab and etesevimab. Sites that have bamlanivimab or etesevimab doses with expired dates must verify the shelf life extension date here.

COVID-19 Therapeutics Information Resources

- **COVID-19 Therapeutics Call Center -** IDPH has established a COVID-19 Therapeutics Call Center. To reach the COVID-19 Therapeutics Call Center, call **515-281-7317**.
- **COVID-19 Therapeutics Email -** IDPH has set up a COVID-19 Therapeutics Email to respond specifically to questions from healthcare providers regarding COVID-19 therapeutics. Therapeutic questions can be emailed to: C19Therapeutics@idph.iowa.gov
- NOTE: **The COVID-19 Therapeutics Call Center and Email are intended for healthcare providers only.**
- **COVID-19 Therapeutics Website -** IDPH is in the process of updating the COVID-19 Therapeutics website with additional resources. Information will be shared as soon as it is available.